
Klf4 Organizes Long-Range Chromosomal Interactions with the Oct4 Locus in Reprogramming and Pluripotency.

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Authors: Zong Wei, Fan Gao, Sewoon Kim, Hongzhen Yang, Jungmook Lyu, Woojin An, Kai Wang, Wange Lu

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Public Summary:

Klf4 is one of the factors that can convert somatic cells to iPS cells. This work describes that the 3D nuclear architecture changes during somatic cell reprogramming and how Klf4 changes the nuclear 3D structure of somatic cells to pluripotent stem cells.

Scientific Abstract:

Epigenetic mechanisms underlying somatic reprogramming have been extensively studied, but little is known about the nuclear architecture of pluripotent stem cells (PSCs). Using circular chromosome conformation capture with high-throughput sequencing (4C-seq) and fluorescence in situ hybridization (FISH), we identified chromosomal regions that colocalize frequently with the Oct4 locus in PSCs. These PSC-specific long-range interactions are established prior to transcriptional activation of endogenous Oct4 during reprogramming to induced PSCs and are facilitated by Klf4-mediated recruitment of cohesin. Depletion of Klf4 leads to unloading of cohesin at the Oct4 enhancer and disrupts long-range interactions prior to loss of Oct4 transcription and subsequent PSC differentiation, suggesting a causative role for Klf4 in facilitating long-range interactions independent of its transcriptional activity. Taken together, our results delineate the basic nuclear organization at the Oct4 locus in PSCs and suggest a functional role for Klf4-mediated higher-order chromatin structure in maintaining and inducing pluripotency.

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